REMARKS

Introduction, Status of Claims & Support for Amendments

Before entry of the present amendments, claims 56-61 were pending and examined on the merits. Upon entry of the present amendments, claim 56 will be canceled without prejudice or disclaimer; claims 57-59 and 61 will be amended; and independent claim 62, claims 63-111 dependent therefrom, independent claim 112 and claims 113-115 dependent therefrom will be added. All claims previously depending (either directly or indirectly) from now canceled claim 56 now depend (either directly or indirectly) from claim 112.

All amendments and new claims are supported by the Specification as originally filed. In particular, support for the language, "and (a) suitable host cell(s) therefor" in claims 58, 59 and 61 can be found, e.g., at page 11, lines 4-7. Support for independent claim 62 and corresponding dependent claims is found, for example, at page 8, lines 30-33 and original claim 22. In claim 112, the preamble language is supported, inter alia, at page 3, lines 31-33 and page 14, lines 8-18; method step "(i)" finds support at, e.g., page 5, lines 7-8; support for step "(ii)" is found, for example, at page 5, line 8; step "(iii)" is supported by, e.g., page 5, lines 5-6; step "(iv)" is supported by, e.g., page 5, lines 10-12; support for step "(v)" exists, for instance, at page 5, lines 20-22, and lines 23-25; and step "(vi)" derives support from page 7, lines 6-8, for example. Support for the phrase, "wherein said plurality of known human immunoglobulin sequences are human [Vκ, Vλ or VH] immunoglobulin sequences" can be found, for example, at page 23, lines 11-13.

The Examiner has rejected the claims as indefinite under 35 U.S.C. § 112, second paragraph, and as anticipated under 35 U.S.C. § 102. In light of the claim

amendments presented herein and the following remarks, withdrawal of all rejections respectfully is requested.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 56, 57 and 59-61 stand rejected as allegedly indefinite. Applicants respectfully submit that those rejections are rendered moot by the instant claim amendments for the reasons set forth below.

The Examiner appears to reject the phrase "a collection of (poly)peptides" in dependent claims 57 and 59-61, on the grounds that former base claim 56 (now corresponding to claim 112) is directed to a single "polypeptide". Applicants respectfully urge that the relationship between the base claim and the corresponding dependent claims is proper. Although base claim 112 is directed to one polypeptide, numerous polypeptides can be produced by the method steps recited therein. Accordingly, dependent claims 57 and 59-61 merely contemplate two or more polypeptides produced according to the methods specified in claim 112. Withdrawal of the rejection is requested.

A "consensus sequence", as recited in step (iv) of claim 112, is clearly defines in the specification of the instant application as "that sequence which comprises the amino acids which are most frequently represented at [a given] position [of a polypeptide]" (Specification at page 13, lines 26-27). Thus, there is no minimum or maximum number of amino acids necessary to define a consensus sequence. Rather, in any collection of related polypeptides, a consensus sequence can be generated for any given stretch of a polypeptide (e.g., for an immunoglobulin

framework sub-region). Accordingly, withdrawal of the rejection respectfully is requested.

The Examiner also questions "which (poly)peptide sub-element is being identified" in step (c) of claim 56, (Office Action at page 2, lines 18-19). Cancellation of claim 56 renders this rejection moot. Step "(ii)" of newly added independent claim 112 recites, "identifying the conserved framework sub-elements of said known and aligned human immunoglobulin sequences". Applicants submit that the foregoing language makes clear the identity of the recited sub-elements.

The Examiner also questions "what constitutes 'setting up' cleavage sites" in step (e) of claim 56 (Office Action at page 2, lines 20-21). Because this language no longer appears in any pending claim, the rejection is moot. Nonetheless, Applicants point out that "cleavage sites," as described in claim 112, are comprised within the nucleic acid molecule at the boundary between each consensus framework sub-element and CDR sub-elements.

Claims 58 and 59 stand rejected as allegedly not being distinguished over base claim 56. Without acquiescing in the Examiner's position, Applicants have added the feature "(a) suitable host cell(s)" to these claims. Accordingly, withdrawal of the rejections respectfully is requested.

Rejections under 35 U.S.C. § 102(e)

Claims 56-72 are rejected under 35 USC §102(e) as anticipated by U.S. Patent No. 5,693,493 issued to Robinson *et al.* ("Robinson"), as well as U.S. Patent No. 5,693,761 issued to Queen *et al.* ("Queen"). Applicants respectfully traverse each of the rejections.

It is axiomatic that, for a prior art reference to be anticipatory, every element of the claimed invention must be identically shown in a single reference. In re Bond, 15 USPQ2d 1566 (Fed. Cir. 1990). In this instance, neither Robinson nor Queen describes every element of the claimed invention; accordingly, neither reference can anticipate the claimed invention.

Robinson

Robinson allegedly describes modular genes encoding antibodies and having consensus sequences of light and heavy chain J regions of an immunoglobulin (see Office Action at page 4, first paragraph). Robinson, however, does not teach or suggest a polypeptide having consensus VH and VL framework sequences, as instantly claimed (claims 62-111); Robinson also fails to teach or suggest a polypeptide that would be produced by the methods recited in the instant claims (claims 112 and 57-61).

Robinson does not teach or suggest, for example, the construction or use of consensus framework sub-regions for an immunoglobulin. First, Robinson never mentions how the so-called "consensus" J-region sequences were generated and, hence, does not teach or suggest, or even enable, the consensus sequence formation steps recited in, e.g., claim 112. In addition, Robinson teaches "consensus" sequences of "light and heavy J regions" of an immunoglobulin (col. 12, lines 57-60) (emphasis added). Robinson defines the "J" region as the "joining" region of the variable and constant regions of an immunoglobulin (col. 12, line 53; Fig. 1). There is no indication that the "J" region contains one or more CDR or framework sub-elements, both or neither. Accordingly, Robinson does not describe immunoglobulin framework sub-elements containing deduced consensus sequences where the consensus sequences can be deduced by comparing amino acids at each

corresponding position of said conserved framework sub-elements, as is required by claims 112 and 57-61 dependent therefrom.

Moreover, the purportedly "modular" genes described by Robinson have a structure that is quite different from the genes that encode the instantly claimed nucleic polypeptides. Robinson describes genes containing restriction sites between the variable region V, D, and J segments. The locations of these restriction sites were necessary because Robinson relied on PCR amplification of naturally occurring variable region fragments to construct the "modular" antibody genes. In other words, individual V, D, and J gene segments were amplified by PCR and the resulting PCR products were ligated together using restriction sites present in the PCR primers.

However, the boundaries between variable region V, D, and J segments are quite different from the boundaries between framework and CDR regions that are the locus of the DNA cleavage sites used in the claimed invention. For example, the V segment used by Robinson contains framework regions 1-3 and CDRs 1 and 2. Accordingly, such V segments do not contain DNA cleavage sites "at the boundary between each consensus framework sub-element and CDR sub-elements," as is recited in the instantly claimed invention. Moreover, this demonstrates that Robinson fails to describe use of consensus sequences for any of framework regions 1-3 as required by the instant claims. Accordingly, Robinson does not describe each and every element of the claimed invention.

Queen

Queen suffers from the same deficiency as Robinson, with respect to the failure to teach polypeptides comprising the consensus framework regions recited in the instant claims. Rather, Queen describes use of long overlapping

oligonucleotides to prepare genes encoding "humanized" antibodies. A humanized antibodies sequence is derived from a non-human (typically murine) antibody sequence by a laborious process of changing a relatively small number of individual amino acid residues at certain positions from residues that are characteristically "non-human" at that position to structurally related residues that are more "human" at that position, all while retaining the binding characteristics of the antibody. This process must be individually "tailored" for any given non-human antibody because the individual amino acid substitutions used in the humanization process necessarily depend on the residues present in the starting non-human antibody. Accordingly, rather than teaching polypeptides containing the types of consensus framework sequences required by the present invention, Queen teaches just the opposite: highly individualized polypeptides having the basic sequence of a non-human antibody that has been modified at certain residues to make the polypeptide more human-like. Accordingly, Queen does not describe each and every limitation of the claimed invention, and withdrawal of the rejection respectfully is requested.

CONCLUSION

In view of the foregoing, Applicants respectfully request the Examiner to withdraw each rejection and pass the claims to allowance. The Examiner is invited to contact the undersigned attorney to resolve any issues, in order to expedite the prosecution of the application.

Respectfully submitted,

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Date

For: Paul M. Booth 31,298
Reg. No. 40,244

Customer ID No. 26633
HELLER EHRMAN WHITE & MCAULIFFE LLP
1666 K Street, NW
Suite 300
Washington, DC 20006
Telephone: (202) 912-2000
Facsimile: (202) 912-2020

Marked-Up Copy of Amended Claims

56. (Canceled) ~~A (poly) peptide comprising an amino acid consensus sequence capable of being identified by the steps of:~~

~~a) deducing from a collection of at least three homologous proteins one or more (poly)peptide sequences comprising at least one amino acid consensus sequence;~~

~~(b) optionally, identifying amino acids in said (poly)peptide sequences to be modified so as to remove unfavorable interactions between amino acids within or between said or other (poly)peptide sequences;~~

~~(c) identifying at least one structural sub-element within each of said (poly)peptide sequences;~~

~~(d) backtranslating each of said (poly)peptide sequences into a corresponding coding nucleic acid sequence;~~

~~(e) setting up cleavage sites in regions adjacent to or between the ends of sub-sequences encoding said sub-elements, each of said cleavage sites:~~

~~(ea) being unique within each of said coding nucleic acid sequences;~~

~~(eb) being common to the corresponding sub-sequences of any said coding nucleic acids.~~

57. (Currently amended) A collection of (poly)peptides comprising a plurality of (poly)peptides according to claim 112~~56~~.

58. (Currently amended) A kit comprising a (poly)peptide according to claim ~~56~~112 and a suitable host cell therefor.

59. (Currently amended) A kit comprising a collection of (poly)peptides

according to claim 57 and suitable host cells therefor.

60. (Currently amended) A collection of (poly)peptides according to claim 57, comprising specific (poly)peptides wherein the genes encoding said specific (poly)peptides

(a) are either homologous, or represent consensus gene sequences derived from at least three homologous genes, and

(b) wherein said ~~carry~~ cleavage sites~~, each of which:~~

(ba) ~~lie at or adjacent to the ends of genetic sub-sequences which encode structural sub-elements,~~

~~(bb)~~ are unique within each gene sequence,

~~(bc)~~ (bb) do not form compatible sites with respect to any single sub-sequence, and

~~(bd)~~ (bc) are common to all homologous sub-sequences.

61. (Currently amended) A kit comprising a collection of (poly) peptides according to claim 60 and suitable host cells therefor.

62. (new) A synthetic antibody molecule comprising a variable heavy chain polypeptide sequence and a variable light chain polypeptide sequence, wherein each of said variable polypeptide sequences comprise four framework regions and three complementarity determining regions, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of a sequence selected from the group consisting of VH1A (SEQ ID NO:57), VH1B (SEQ ID NO:59), VH2 (SEQ ID NO:61), VH3 (SEQ ID NO:63), VH4 (SEQ ID NO:65), VH5 (SEQ ID NO:67), and VH6 (SEQ ID NO:69), and wherein the four framework regions

of said variable light chain comprise the corresponding framework regions of a sequence selected from the group consisting of Vκ1 (SEQ ID NO: 43), Vκ2 (SEQ ID NO: 45), Vκ3 (SEQ ID NO: 47), Vκ4 (SEQ ID NO: 49), Vλl (SEQ ID NO: 51), Vλ2 (SEQ ID NO: 53), and Vλ3 (SEQ ID NO: 55).

63. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1A (SEQ ID NO:57), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ1 (SEQ ID NO: 43).

64. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1A (SEQ ID NO:57), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ2 (SEQ ID NO: 45).

65. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1A (SEQ ID NO:57), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ3 (SEQ ID NO: 47).

66. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise he corresponding

framework regions of VH1A (SEQ ID NO:57), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ4 (SEQ ID NO: 49).

67. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1A (SEQ ID NO:57), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλl (SEQ ID NO: 51).

68. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1A (SEQ ID NO:57), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλ2 (SEQ ID NO: 53).

69. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1A (SEQ ID NO:57), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλ3 (SEQ ID NO: 55).

70. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1B (SEQ ID NO:59), and wherein the four framework

regions of said variable light chain comprise the corresponding framework regions of Vκ1 (SEQ ID NO: 43).

71. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1B (SEQ ID NO:59), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ2 (SEQ ID NO: 45).

72. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1B (SEQ ID NO:59), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ3 (SEQ ID NO: 47).

73. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1B (SEQ ID NO:59), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ4 (SEQ ID NO: 49).

74. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1B (SEQ ID NO:59), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of

Vλ1 (SEQ ID NO: 51).

75. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1B (SEQ ID NO:59), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλ2 (SEQ ID NO: 53).

76. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1B (SEQ ID NO:59), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλ3 (SEQ ID NO: 55).

77. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH2 (SEQ ID NO:61), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ1 (SEQ ID NO: 43).

78. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH2 (SEQ ID NO:61), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ2 (SEQ ID NO: 45).

79. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH2 (SEQ ID NO:61), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ3 (SEQ ID NO: 47).

80. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH2 (SEQ ID NO:61), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ4 (SEQ ID NO: 49).

81. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH2 (SEQ ID NO:61), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλl (SEQ ID NO: 51).

82. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH2 (SEQ ID NO:61), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλ2 (SEQ ID NO: 53).

83. (new) The synthetic antibody molecule according to claim 62, wherein the

four framework regions of said variable heavy chain comprise the corresponding framework regions of VH2 (SEQ ID NO:61), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλ3 (SEQ ID NO: 55).

84. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH3 (SEQ ID NO:63), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ1 (SEQ ID NO: 43).

85. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH3 (SEQ ID NO:63), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ2 (SEQ ID NO: 45).

86. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH3 (SEQ ID NO:63), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ3 (SEQ ID NO: 47).

87. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding

framework regions of VH3 (SEQ ID NO:63), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ4 (SEQ ID NO: 49).

88. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH3 (SEQ ID NO:63), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλl (SEQ ID NO: 51).

89. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH3 (SEQ ID NO:63), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλ2 (SEQ ID NO: 53).

90. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH3 (SEQ ID NO:63), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλ3 (SEQ ID NO: 55).

91. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH4 (SEQ ID NO:65), and wherein the four framework regions

of said variable light chain comprise the corresponding framework regions of Vκ1 (SEQ ID NO: 43).

92. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH4 (SEQ ID NO:65), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ2 (SEQ ID NO: 45).

93. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH4 (SEQ ID NO:65), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ3 (SEQ ID NO: 47).

94. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH4 (SEQ ID NO:65), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ4 (SEQ ID NO: 49).

95. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH4 (SEQ ID NO:65), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλl

(SEQ ID NO: 51).

96. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH4 (SEQ ID NO:65), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλ2 (SEQ ID NO: 53).

97. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH4 (SEQ ID NO:65), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλ3 (SEQ ID NO: 55).

98. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH5 (SEQ ID NO:67), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ1 (SEQ ID NO: 43).

99. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH5 (SEQ ID NO:67), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ2 (SEQ ID NO: 45).

100. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH5 (SEQ ID NO:67), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ3 (SEQ ID NO: 47).

101. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH5 (SEQ ID NO:67), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ4 (SEQ ID NO: 49).

102. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH5 (SEQ ID NO:67), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλl (SEQ ID NO: 51).

103. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH5 (SEQ ID NO:67), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλ2 (SEQ ID NO: 53).

104. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH5 (SEQ ID NO:67), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλ3 (SEQ ID NO: 55).

105. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH6 (SEQ ID NO:69), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ1 (SEQ ID NO: 43).

106. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH6 (SEQ ID NO:69), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ2 (SEQ ID NO: 45).

107. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH6 (SEQ ID NO:69), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ3 (SEQ ID NO: 47).

108. (new) The synthetic antibody molecule according to claim 62, wherein the

four framework regions of said variable heavy chain comprise the corresponding framework regions of VH6 (SEQ ID NO:69), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vκ4 (SEQ ID NO: 49).

109. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH6 (SEQ ID NO:69), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλl (SEQ ID NO: 51).

110. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH6 (SEQ ID NO:69), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλ2 (SEQ ID NO: 53).

111. (new) The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH6 (SEQ ID NO:69), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of Vλ3 (SEQ ID NO: 55).

112. (new) An immunoglobulin polypeptide comprising four amino acid consensus framework sub-elements and having interspaced complementarity determining

region (CDR) sub-elements, wherein said polypeptide is produced by the steps of: (i) aligning a plurality of known human immunoglobulin sequences; (ii) identifying the conserved framework sub-elements of said known and aligned human immunoglobulin sequences; (iii) comparing amino acids at each corresponding position of said conserved framework sub-elements; (iv) deducing consensus sequences for the framework sub-elements based on said comparing step (iii); (v) synthesizing a nucleic acid molecule capable of encoding said polypeptide, wherein said nucleic acid molecule comprises DNA cleavage sites at the boundary between each consensus framework sub-element and CDR sub-elements; and (vi) allowing the expression of said synthesized DNA molecule as said immunoglobulin polypeptide.

113. (New) The immunoglobulin polypeptide according to claim 112, wherein said plurality of known human immunoglobulin sequences are human Vκ immunoglobulin sequences.

114. (New) The immunoglobulin polypeptide according to claim 112, wherein said plurality of known human immunoglobulin sequences are human Vλ immunoglobulin sequences.

115. (New) The immunoglobulin polypeptide according to claim 112, wherein said plurality of known human immunoglobulin sequences are human VH immunoglobulin sequences.